S ogywarae cacaaca

1 (After amendment). A pyrazole derivative represented by the following general formula (I) or a pharmaceutically acceptable salt thereof

$$\begin{array}{c|c}
N & D & CH_2 \\
\hline
 & B & X-A (I)
\end{array}$$

(in the formula, each symbol has the following meaning;
D: pyrazolyl which may have to 3 substituents selected
from the group consisting of Alk, -lower alkenyl, -lower
alkynyl, -halogeno-lower alkyl, -Alk-cycloalkyl,
-Alk-O-Alk, -cycloalkyl, -O-Alk, -COOH, -COO-Alk and -Hal,
n: 0 or 1,

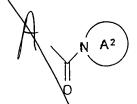
B: phenylene, a nitrogen-containing, divalent, saturated ring group, or a monocyclic, divalent heteroaromatic ring group which may be substituted with Alk,

 $X: -NR^{1}-CR^{2}R^{3}-, -CR^{2}R^{3}-NR^{1}-, -NR^{1}-SO_{2}-, -SO_{2}-NR^{1}-$ or $-CR^{4}=CR^{5}-,$ $R^{1}: -H, -OH, -Alk, -O-Alk$ or -CO-Alk,

 R^2 and R^3 : the same or different from each other and each represents -H or -Alk, or R^2 and R^3 together form =0 or =S, R^4 and R^5 : the same or different from each other and each represents -H, -Hal, -halogeno-lower alkyl or -Alk, and

A: benzene ring which may have one or more substituents; mono-, di- or tricyclic fused heteroaryl which may have one or more substituents; cycloalkyl which may have one or more substituents; a nitrogen-containing, saturated ring group which may have one or more substituents; lower alkenyl which may have one or more substituents; lower alkynyl which may have one or more substituents; or Alk which may have one or more substituents, or A and X may together form a group represented by a formula

Sub A9

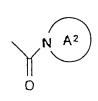


(wherein A² is a nitrogen-containing hetero ring selected from the group consisting of 1-pyrrolidinyl, pyrazolidinyl, piperidino, piperazinyl, morpholino, 3,4-dihydro-2H-1,4-benzoxazin-4-yl and indolinyl, wherein said hetero ring may have one or more substituents), with the proviso that

- (1) when D is 3,5-bis(trifluoromethyl)-1ki-pyrazol-1-yl, n is 0, B is 1,4-phenylene and X is NHCO, A is a group other than 4-methyl-1,2,3-thiadiazol-5-yl,
- (2) when D is 1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl, n is 0, B is thiophene-2,5-diyl and X is CONH, A is a group other than 4-chlorophenyl,

- (%) when D is 1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl, n is 0, B is thiophene-2,5-diyl and X is CONH, A is a group other than benzyl,
- (4) when D is 4-ethoxycarbonyl-5-trifluoromethyl-1H-pyrazol-1-yl, n is 0, B is 1,4-phenylene and Y is NHCO, A is a group other than trichlorovinyl,
- (5) when D is 1H-pyrazol-1-yl, n is 0, B is 1,4-phenylene and Y is NHCO. A is a group other than 2-ethoxyvinyl, and (6) when n is 1 D is 1H-pyrazol-5-yl substituted with at least one trifluoromethyl group or 1H-pyrazol-1-yl substituted with at least one trifluoromethyl group).
- 2. The pyrazole derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein A is phenyl which may have one or more substituents of F group; mono-, di- or tricyclic fused heteroaryl which may have one or more substituents of $\backslash F$ group; cycloalkyl which may have one or more substituents of F group; a nitrogencontaining, saturated ring group which may have one or more substituents of F group; lower alkenyl which may have one or more substituents of G group; lower alkynyl which may have one or more substituents of G group; or Alk which may have one or more substituents of $\backslash\! G$ group, wherein the F group is a group consisting of -\lambdalk, -lower alkenyl, -lower alkynyl, -Hal, -NH₂, -NH(Alk), -N(Alk)₂, -NO₂, -CN, -OH, -O-Alk, -O-CO-Alk, -SH, -S-Alk, -COO+1, -COO-Alk, -CO-Alk, -CHO, -CONH₂, -CONH(Alk), -CON(Alk) $_2$, -SO-Alk, $-SO_2-Alk$, $-SO_2NH_2$, $-SO_2NH-(Alk)$, $-SO_2N(Alk)_2$, +aryl, -cycloalkyl, -O-Alk-O-, -halogeno-lower alkyl λ -Alk-NH₂, -Alk-NH(Alk), -Alk-N(Alk)₂, -Alk-OH, -Alk-O-Alk, -Alk-SH,

-Alk-S-Alk, -Alk-COOH, -Alk-COO-Alk, -Alk-CO-Alk, -Alk-CHO, -Alk-CONH₂, -Alk-CONH(Alk), -Alk-CON(Alk)₂, -Alk-SO-Alk, -Alk-SO₂-Alk, -Alk-SO₂NH₂, -Alk-SO₂NH(Alk), -Alk-SON(Alk)2, -Alk-aryl and -Alk-cycloalkyl, and the G group is a group consisting of -Hal, $-NH_2$, -NH(Alk), $-N(Alk)_2$, $-NQ_2$, -CN, -OH, -O-Alk, -O-CO-Alk, -SH, -S-Alk, -COOH, -COO-Alk, -COO, -CONH₂, -CONH(Alk), $-CON(Alk)_2$, -SO-Alk, $-SO_2-Alk$, $-SO_2NH_2$, $-SO_2NH-(Alk)$, -SO₂N(Alk)₂, aryl which may have one or more substituents of F group; mono-, di-n or tricyclic fused heteroaryl which may have one or more supstituents of F group; cycloalkyl which may have one or more substituents of F group and a nitrogen-containing, saturated ring group which may have one or more substituents of F group, or A and X may together form a group represented by a formula



(wherein A^2 is a nitrogen-containing hetero ring selected from the group consisting of 1-pyrrolidinyl, pyrazolidinyl, piperidino, 1-piperazinyl, morpholino, 3,4-dihydro-2H-1,4-benzoxazin-4-yl and indolinyl, wherein said hetero ring may have one or more substituents of F group).

The pyrazole derivative or pharmaceutically acceptable salt thereof according to claim 2, wherein B is phenylene; piperidine-1,4-diyl; or a monocyclic, divalent heteroaromatic ring group selected from the class consisting of thiophene, furan, pyrrole, imidazole, pyrazole, thiazolè, isothiazole, oxazole, isoxazole, thiadiazole, pyridine, pyrazine, pyridazine and pyrimidine, which may be substituted with Alk, X is -NH-CO-, $-NH-CH_2-$, -N(OH)-CO-, -N(Alk)-CO-, -CO-NH-, $-CH_2-NH-$, -CO-N(OH)-, -CO-N(Alk)-, $-SO_2NH-$, $-NHSO_2-$ or -CH=C(Hal)-,A is aryl which may have one or more substituents of group F; mono-, di- or tricyclic fused heteroaryl selected from the group consisting of thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, tetrazolyl, triazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, isoindolyl, isoquinolyl, quinolyl, quinoxanyl, phthalazinyl, imidazopyridyl, quinazolinyl and cinnolinyl, which may have one or more substituents of group F; cycl\alkyl; a nitrogen-containing, saturated ring selected from the group consisting of pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperidyl, piperazinyl and morpholinyl, which may be substituted with one or more Alk; lower alkynyl which may be substituted with one or more Hal) lower alkenyl which may be substituted with one or more

Hal; or Alk which may be substituted with one or more Hal, and

the F group is a group consisting of -Alk, -lower alkenyl,

-lower alkynyl, -Hal, -NH₂, -NH(Alk), -N(Alk)₂, -NO₂, -CN,

-OH, -O-Alk, -O-CO-Alk, -SH, -S-Alk, -COOH, -COO-Alk,

-CO-Alk, -CHO, $-CONH_2$, -CONH(Alk), -CON(Alk), -SO-Alk,

 $-SO_2-Alk$, $\sqrt{SO_2NH_2}$, $-SO_2NH-(Alk)$ and $-SO_2N(Alk)_2$,

or A and X may together form a group represented by a formula

509) 49

4 (after amendment). The pyrazole derivative or pharmaceutically acceptable salt thereof according to claim 3, wherein

n is 0, D is pyrazolyl which may have 1 to 3 substituents selected from -Alk, -halogeno-lower alkyl, -COOH and -COO-Alk,

B is phenylene or a monocyclic, divalent heteroaromatic ring group selected from the class consisting of thiophene, furan, thiazole, pyridine and pyrimidine, which may be substituted with Alk,

X is -NH-CO-, -N(OH)-CO-, -CO-NH-, $-CH_2-NH$ or -CO-N(Alk)-, and

A is phenyl which may have one or more substituents selected from the group consisting of -Alk, -Hal -NH₂, -N(Alk)₂, -NO₂, -CN, -OH, -O-Alk and -COO-Alk; mono,

sih Ra di or tricyclic fused heteroaryl selected from the group consisting of thienyl, pyrrolyl, imidazolyl, thiazolyl, oxazolyl, tetrazolyl, triazolyl, thiadiazolyl, pyridyl, pyrazinyl and isoquinolyl, which may be substituted with Alk; cycloalkyl; lower alkenyl which may be substituted with one or more Hal; or Alk.

500 ac7

- 5. The pyrazole derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein D is pyrazolyl substituted with at least one trifluoromethyl group.
- 6. The pyrazole derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein D is 1H-pyrazol-5-yl substituted with at least one trifluoromethyl group or 1H-pyrazol-1-yl substituted with at least one trifluoromethyl group.
- 7. The pyrazole derivative or pharmaceutically acceptable salt thereoff according to claim 1, wherein X is -NH-CO- or -CO-NH-.
- 8. The pyrazole derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein D is 1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl and A is phenyl which may be substituted with Hal.

5 U/2

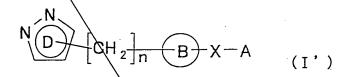
9. The pyrazole derivative or pharmaceutically acceptable salt thereof according to claim 1, wherein D is 3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl and A is monocyclic heteroaryl selected from the group consisting

Sub (3

of thiazolyl, thiadiazolyl, thienyl and pyridyl, which may be substituted with Alk.

10 (after amendment). A pharmaceutical composition which comprises a pyrazole derivative represented by the following general formula (I') or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier

SUB



(in the formula, each symbol has the following meaning;
D: pyrazolyl which may have to 3 substituents selected
from the group consisting of -Alk, -lower alkenyl, -lower
alkynyl, -halogeno-lower alkyl, Alk-cycloalkyl,
-Alk-O-Alk, -cycloalkyl, -O-Alk, -COOH, -COO-Alk and -Hal,
n: 0 or 1,

B: phenylene, a nitrogen-containing, divalent, saturated ring group, or a monocyclic, divalent heteroaromatic ring group which may be substituted with Alk,

X: $-NR^{1}-CR^{2}R^{3}-$, $-CR^{2}R^{3}-NR^{1}-$, $-NR^{1}-SO_{2}-$, $-SO_{2}-NR^{1}$ or $-CR^{4}=CR^{5}-$, R^{1} : -H, -OH, -Alk, -O-Alk or -CO-Alk,

 R^2 and R^3 : the same or different from each other and each represents -H or -Alk, or R^2 and R^3 together form =0 or =S, R^4 and R^5 : the same or different from each other and each represents -H, -Hal, -halogeno-lower alkyl or -Alk, and

A: benzene ring which may have one or more substituents; mono di- or tricyclic fused heteroaryl which may have one or more substituents; cycloalkyl which may have one or more substituents; a nitrogen-containing, saturated ring group which may have one or more substituents; lower alkenyl which may have one or more substituents; lower alkynyl which may have one or more substituents; or Alk which may have one or more substituents; or Alk which may have one or more substituents, or A and X may together form a group represented by a formula

N A^2

(wherein A² is a nitrogen-containing hetero ring selected from the group consisting of 1-pyrrolidinyl, pyrazolidinyl, piperidino, piperazinyl, morpholino, 3,4-dihydro-2H-1,4-benzoxazin-4-yl and indolinyl, wherein said hetero ring may have one or more substituents), with the proviso that when n is 1, D is 1H-pyrazol-5-yl substituted with at least one trifluoromethyl group or 1H-pyrazol-1-yl substituted with at leaset one trifluoromethyl group).

- 11. The pharmaceutical composition according to claim 10, which is a calcium release-dependent calcium channel inhibitor.
- 12. The pharmaceutical composition according to claim 11, which is an IL-2 production inhibitor.

- 13. The pharmaceutical composition according to claim 12, which is a preventive or therapeutic agent for allergic, inflammatory or autoimmune diseases.
- 14. The pharmaceutical composition according to claim 13, which is a preventive or therapeutic agent for bronchial asthma or rheumatoid arthritis.
- 15. The pharmaceutical composition according to claims 10 to 14, wherein D is pyrazolyl substituted with at least one trifluoromethyl group.
- 16. The pharmaceutical composition according to claims 10 to 14, wherein D is H-pyrazol-5-yl substituted with at least one trifluoromethyl group or 1H-pyrazol-1-yl substituted with at least one trifluoromethyl group.
- 17. The pharmaceutical composition according to claims 10 to 14, wherein X is -NH-CO- or -CO-NH-.
- 18. The pharmaceutical composition according to claims 10 to 14, wherein D is 1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl and A is phenyl which may be substituted with Hal.
- 19. The pharmaceutical composition according to claims 10 to 14, wherein D is 3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl and A is monocyclic heteroaryl selected from the group consisting of thiazolyl, thiadiazolyl, thienyl and pyridyl, which may be substituted with Alk.

add
A12
add
B2

71